CLAIMS

1. Compounds of formula (I):

$$\begin{array}{c|c} Z & O & (CH_2) - N \\ \hline & & \\ W_1 & & \\$$

wherein:

5

10

15

- W₁ represents, with the carbon atoms to which it is attached, a phenyl group or a pyridyl group,
- **Z** represents a group selected from hydrogen, halogen, and the groups linear or branched (C₁-C₆)alkyl, aryl, aryl-(C₁-C₆)alkyl in which the alkyl moiety may be linear or branched, aryloxy, aryl-(C₁-C₆)alkoxy in which the alkoxy moiety may be linear or branched, hydroxy and linear or branched (C₁-C₆)alkoxy,
- R₁ represents a group selected from hydrogen and the groups linear or branched (C₁-C₆)alkyl, aryl, aryl-(C₁-C₆)alkyl in which the alkyl moiety may be linear or branched, -C(O)-R₅ and a linear or branched (C₁-C₆)alkylene chain, which are substituted by one or more identical or different groups selected from halogen and the groups cyano, -OR₆, -NR₆R₇, -CO₂R₆, -C(O)R₆ and -C(O)-NHR₆, wherein:
 - \Rightarrow R₅ represents a group selected from hydrogen and the groups linear or branched (C₁-C₆)alkyl, hydroxy, linear or branched (C₁-C₆)alkoxy, aryl, aryl-(C₁-C₆)alkyl in which the alkyl moiety may be linear or branched and aryloxy,
 - ⇒ R₆ and R₇, which may be identical or different, each represents a group selected from hydrogen and the groups linear or branched (C₁-C₆)alkyl, aryl and aryl-(C₁-C₆)alkyl in which the alkyl moiety may be linear or branched, or

 $R_6 + R_7$ together form, with the nitrogen atom carrying them, a monocyclic heterocycle having 5 or 6 ring members and optionally containing in the ring system a second hetero atom selected from oxygen and nitrogen,

- R₂ represents a hydrogen atom or a group of formula -CH₂CH₂O-R₈ wherein:
 R₈ represents a group selected from hydrogen and the groups linear or branched (C₁-C₆)alkyl, aryl, aryl-(C₁-C₆)alkyl in which the alkyl moiety may be linear or branched, -S(O)_t-R₆ (wherein R₆ is as defined hereinbefore and t represents an integer of from 0 to 2 inclusive) and T₁-R₉ (wherein T₁ represents a linear or branched (C₁-C₆)alkylene chain and R₉ represents a group selected from halogen, cyano, -OR₆, -NR₆R₇, -C(O)H, -C(O)OR₆ and -C(O)NR₆R₇, wherein R₆ and R₇ are as defined hereinbefore),
 - R₃ and R₄, which may be identical or different, each represents, independently of the other, a group selected from hydrogen and the groups linear or branched (C₁-C₆)alkyl, aryl and aryl-(C₁-C₆)alkyl in which the alkyl moiety may be linear or branched, or R₃ and R₄ together form, with the nitrogen atom carrying them, a monocyclic heterocycle having 5 or 6 ring members and optionally containing in the ring system a second hetero atom selected from oxygen and nitrogen,
 - n represents an integer of from 1 to 6 inclusive,

15

20

25

their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base,

wherein "aryl" is to be understood as meaning a phenyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, indenyl or indanyl group, each of those groups being optionally substituted by one or more identical or different groups selected from halogen, linear or branched (C_1-C_6) alkyl, linear or branched (C_1-C_6) alkyl, hydroxy, linear or branched (C_1-C_6) alkoxy, and amino optionally substituted by one or two linear or branched (C_1-C_6) alkyl groups.

2. Compound of formula (I) according to claim 1, characterised in that they represent compounds of formula (IA):

$$Z \longrightarrow O \longrightarrow (CH_2) - N \longrightarrow R_3$$

$$W_1 \longrightarrow O \longrightarrow R_4$$

$$R_1 \longrightarrow O \longrightarrow R_2$$
(IA)

wherein R₁, R₂, R₃, R₄, W₁, Z and n are as defined for formula (I), their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.

3. Compounds of formula (I) according to either claim 1 or claim 2, characterised in that they represent compounds of formula (IB):

$$Z \xrightarrow{O} \xrightarrow{CCH_2) - N} \xrightarrow{R_3} \qquad (IB)$$

10

wherein R_1 , R_2 , R_3 , R_4 , Z and n are as defined hereinbefore, their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.

4. Compounds of formula (I) according to either claim 1 or claim 2, characterised in that they represent compounds of formula (IC):

$$Z \xrightarrow{O} \xrightarrow{O} \xrightarrow{(CH_2) - N} \xrightarrow{R_3} \xrightarrow{R_4}$$

$$Z \xrightarrow{N} \xrightarrow{N} \xrightarrow{O} \xrightarrow{R_2}$$

$$(IC)$$

wherein R_1 , R_2 , R_3 , R_4 , Z and n are as defined hereinbefore, their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.

- 5 Compounds of formula (I) according to any one of claims 1 to 4, characterised in that Z represents a hydrogen atom, their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.
 - 6. Compounds of formula (I) according to any one of claims 1 to 5, characterised in that R₁ represents a hydrogen atom or a -C(O)-R₅ group wherein R₅ represents more especially a hydrogen atom, their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.

10

- 7. Compounds of formula (I) according to any one of claims 1 to 6, characterised in that R₂ represents a hydrogen atom or a -CH₂CH₂O-R₈ group wherein R₈ represents more especially a hydrogen atom, their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.
- 8. Compounds of formula (I) according to any one of claims 1 to 7, characterised in that n represents an integer 2, their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.
- 9. Compounds of formula (I) according to any one of claims 1 to 8, characterised in that
 20 R₃ and R₄, which may be identical or different, each represents independently of the
 other a linear or branched (C₁-C₆)alkyl group, their enantiomers, diastereoisomers,

N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.

10. Compounds of formula (I) according to claim 1 which are:

5

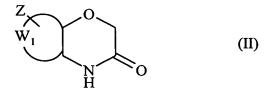
10

15

- 2-[2-(dimethylamino)ethyl]-5-hydroxybenzo[a]pyrrolo[3,4-c]phenoxazine-1,3-dione,
- 2-[2-(diethylamino)ethyl]-5-hydroxybenzo[a]pyrrolo[3,4-c]phenoxazine-1,3-dione,
- 2-[2-(dimethylamino)ethyl]-5-(2-hydroxyethoxy)-2,3-dihydrobenzo[a]pyrrolo[3,4-c]phenoxazine-8-carbaldehyde-1,3-dione,
- 2-[2-(dimethylamino)ethyl]-5-(2-hydroxyethoxy)benzo[a]pyrrolo[3,4-c]-phenoxazine-1,3-dione,
- 2-[2-(dimethylamino)ethyl]-5-(2-hydroxyethylmethanesulphonate)benzo[a]pyrrolo[3,4-c]phenoxazine-1,3-dione,
- 2-[2-(dimethylamino)ethyl]-5-(2-hydroxyethoxy)benzo[e]pyrido[2',3':5,6][1,4]-oxazino[3,2-g]isoindole-1,3-dione,

their enantiomers, diastereoisomers, N-oxide, and addition salts thereof with a pharmaceutically acceptable acid or base.

11. Process for the preparation of compounds of formula (I) according to claim 1, characterised in that there is used as starting material a compound of formula (II):



wherein W_I and Z are as defined for formula (I), the amine function of which compound of formula (II) is protected by a protecting group P_G well known to the person skilled in the art to yield a compound of formula (III):

$$V_{\text{I}} = V_{\text{O}}$$

wherein P_G represents a tert-butoxycarbonyl or phenoxycarbonyl group and W_1 and Z are as defined hereinbefore,

which compound of formula (III) is treated with lithium diisopropylamide followed by diphenyl chlorophosphate to yield a compound of formula (IV):

$$V_{1} \longrightarrow V_{O} \longrightarrow V_{P(OPh)_{2}}$$
 (IV)

wherein P_G, W₁ and Z are as defined hereinbefore,

which compound of formula (IV) is treated, in the presence of bis(triphenyl-phosphine)palladium chloride, with a compound of formula (V):

to yield a compound of formula (VI):

5

10

15

$$\begin{array}{c|c}
Z & O \\
W_1 & P_G
\end{array}$$
(VI)

wherein P_G , W_I and Z are as defined hereinbefore, which compound of formula (VI) is:

• either treated under an inert atmosphere with dimethyl acetylenedicarboxylate to yield a compound of formula (VII):

$$Z \longrightarrow O \longrightarrow COOMe \\ W_1 \longrightarrow P_G \longrightarrow O \longrightarrow O$$

$$(VII)$$

wherein P_G , W_I and Z are as defined hereinbefore, which compound of formula (VII) is:

5

• either treated with N-bromosuccinimide and benzoyl peroxide to yield a compound of formula (VIII):

$$Z \longrightarrow O \longrightarrow COOMe \\ W_1 \longrightarrow P_G \longrightarrow O \longrightarrow COOMe$$

$$VIII)$$

wherein P_G, W₁ and Z are as defined hereinbefore,

which compound of formula (VIII) is subjected to the action of hydrochloric acid to yield a compound of formula (IX):

$$Z \longrightarrow COOMe \\ W_1 \longrightarrow COOMe \\ H \longrightarrow O$$
 (IX)

wherein W₁ and Z are as defined hereinbefore,

which compound of formula (IX) is subjected to the action of di-tert-butyl dicarbonate in the presence of 4-dimethylaminopyridine to yield a compound of formula (X):

wherein _____ represents a single or double bond, Boc represents a tert-butoxycarbonyl group and W_1 and Z are as defined hereinbefore,

which compound of formula (X) is subjected to the action of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to yield a compound of formula (XI):

wherein Boc, W₁ and Z are as defined hereinbefore,

which compound of formula (XI) is subjected to the action of sodium methanolate and is then hydrolysed to yield a compound of formula (XII):

10

5

wherein Boc, W₁ and Z are as defined hereinbefore,

which compound of formula (XII) is subjected to the action of a compound of formula (XIII):

$$H_2N$$
— $(CH_2)_n$ - N
 R_4
(XIII)

wherein R₃, R₄ and n are as defined for formula (I), to yield a compound of formula (I/a), a particular case of the compounds of formula (I):

$$Z \longrightarrow O \longrightarrow N$$

$$V \longrightarrow V \longrightarrow R_{4}$$

$$V \longrightarrow V \longrightarrow N$$

wherein Boc, R₃, R₄, W₁, Z and n are as defined hereinbefore,

which compound of formula (I/a) is optionally subjected to the same reaction conditions as the compound of formula (VIII) to yield a compound of formula (I/b), a particular case of the compounds of formula (I):

$$\begin{array}{c|c} & & & & \\ & & & \\ Z & & & \\ W_1 & & & \\ W_1 & & & \\ & & & \\ W_1 & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

wherein R₃, R₄, W₁, Z and n are as defined hereinbefore,

• or subjected to the same reaction conditions as the compound of formula (X) to yield a compound of formula (XIV):

$$Z \longrightarrow O \longrightarrow COOMe \\ W_1 \longrightarrow O \longrightarrow OH$$
 (XIV)

wherein P_G, W₁ and Z are as defined hereinbefore,

which compound of formula (XIV) is subjected to the same reaction conditions as the compound of formula (XII) to yield a compound of formula (I/c), a particular case of the compounds of formula (I):

10

wherein P_G , R_3 , R_4 , W_1 , Z and n are as defined hereinbefore, which compound of formula (I/c) is :

5

10

either optionally subjected to the action of formic acid to yield compounds of formulae (I/d) and (I/e), particular cases of the compounds of formula (I):

$$Z = \begin{pmatrix} O & (CH_2)_n - N \\ N & Q & (CH_2)_n - N \\ N & Q & Q & (CH_2)_n - N \\ N & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_2 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_2 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_2 & Q & Q & Q & Q \\ W_3 & Q & Q & Q & Q \\ W_4 & Q & Q & Q & Q \\ W_1 & Q & Q & Q & Q \\ W_2 & Q & Q & Q & Q \\ W_3 & Q & Q & Q & Q \\ W_4 & Q & Q & Q & Q \\ W_5 & Q$$

wherein R₃, R₄, W₁, Z and n are as defined hereinbefore,

or optionally subjected to the action of a compound of formula (XV):

$$R_{8a} - G$$
 (XV)

wherein G represents a leaving group and R_{8a} , which is other than a hydrogen atom, has the same definition as R_8 in formula (I), to yield a compound of formula (I/f), a particular case of the compounds of formula (I):

wherein P_G, R₃, R₄, R_{8a}, W₁, Z and n are as defined hereinbefore,

5

10

the amine function of which compounds of formula (I/f) is optionally deprotected according to conventional methods of organic synthesis to yield a compound of formula (I/g), a particular case of the compounds of formula (I):

$$Z \longrightarrow O \longrightarrow O \longrightarrow R_{4}$$

$$W_{1} \longrightarrow O \longrightarrow O \longrightarrow OR_{8a}$$

$$(I/g)$$

wherein R₃, R₄, R_{8a}, W₁, Z and n are as defined hereinbefore,

the compounds of formulae (I/b), (I/d) and (I/g) constituting the compounds of formula (I/h):

$$Z \longrightarrow O \longrightarrow (CH_2)_n \longrightarrow R_3$$

$$W_1 \longrightarrow O \longrightarrow R_4$$

$$W_1 \longrightarrow O \longrightarrow R_4$$

$$O \longrightarrow CI/h$$

$$OR_2$$

wherein R_2 , R_3 , R_4 , W_1 , Z and n are as defined hereinbefore,

which compounds of formula (I/h) are optionally subjected to the action of a compound of formula (XVI):

$$R_{1a} - G$$
 (XVI)

wherein R_{1a} , which is other than a hydrogen atom, has the same definition as R_1 in formula (I) and G is as defined hereinbefore, to yield a compound of formula (I/i), a particular case of the compounds of formula (I):

wherein R_{1a}, R₂, R₃, R₄, W₁, Z and n are as defined hereinbefore,

5

10

• or treated with N-methylmaleimide to yield a compound of formula (XVII):

$$Z \longrightarrow O \longrightarrow N$$

$$W_1 \longrightarrow P_G$$

$$(XVII)$$

wherein P_G, W₁ and Z are as defined hereinbefore,

which compound of formula (XVII) is subjected to the same reaction conditions as the compound of formula (VII) to yield a compound of formula (XVIII):

$$Z \longrightarrow O \longrightarrow O \\ W_1 \longrightarrow O \\ P_G \longrightarrow O \longrightarrow OH$$
 (XVIII)

wherein P_G, W₁ and Z are as defined hereinbefore,

which compound of formula (XVIII) is subjected to the same reaction conditions as the compound of formula (XII) to yield a compound of formula (I/d) as described hereinbefore,

the compounds of formulae (I/a) to (I/i) constituting the totality of the compounds of formula (I), which compounds are optionally purified according to conventional purification techniques, may, if desired, be separated into their different isomers according to a conventional separation technique and are, if desired, converted into their N-oxides and, optionally, into addition salts with a pharmaceutically acceptable acid or base.

- 12. Pharmaceutical compositions comprising as active ingredient at least one compound of formula (I) according to any one of claims 1 to 10, on its own or in combination with one or more pharmaceutically acceptable inert, non-toxic excipients or carriers.
- 13. Pharmaceutical compositions according to claim 12, for use as medicaments in the treatment of cancers.
 - 14. Compounds of formula (X), (XI) and (XIV):

COOMe COOMe
$$X_1$$
 X_2 X_3 X_4 X_4 X_4 X_4 X_5 X_4 X_5 X_5 X_6 X_6 X_6 X_7 X_8 X_8

for use as synthesis intermediates of compounds of formula (I).